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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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AFFYMETRIX, INC			KAPUSHOC, STEPHEN THOMAS	
ATTN: CHIEF IP COUNSEL, LEGAL DEPT.			ART UNIT	PAPER NUMBER
3420 CENTRAL EXPRESSWAY				
SANTA CLARA, CA 95051			1634	

DATE MAILED: 04/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/719,956	ZHOU, XUE MEI	
	Examiner	Art Unit	
	Stephen Kapushoc	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 24 February 2006.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1 and 4-16 is/are pending in the application.
 - 4a) Of the above claim(s) 7-12 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1, 4-6, 13-16 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date: _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>6/04</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1, and 4-16 are pending.

Claims 7-12 are withdrawn

Claims 1, 4-6, 13-16 are examined on the merits

Election/Restrictions

1. Applicant's election without traverse of Group I, pending claims 1, 4-6, and 13-16 in the reply filed on 02/24/2006 is acknowledged.

Specification

2. The title of the invention, 'Methods of genetic analysis of rat', is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.
3. The disclosure is objected to because of the following informalities:

The specification of the instant application discloses a microarray containing probes derived from rat gene and EST sequences (p.3 Ins.5-10; p.18 Ins.27-30). However, page 17 lines 27-29 of the instant specification indicates that 30,000 mouse genes are analyzed, and p.25 Ins.9-11 indicate that SNPs in the mouse genome are analyzed.

Page 25 line 9 of the instant specification teaches an embodiment of an array comprising SEQ ID NOs 1-982,914. However, the sequence listing of the instant specification discloses only SEQ ID NOs: 1-699,466.

Appropriate correction is required.

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4. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See for example page 19. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claims 1, 4-6, and 13-16 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility.

The claims are drawn to an array comprising a plurality of nucleic acid probes. Claims 1 and 4-6 are drawn to an array in which the probes are comprised of the sequences disclosed as SEQ ID NOs: 1-699,466. Claims 13-16 are broadly drawn to an array with at least one probe to each of at least 20,000 different rat transcripts.

The specification teaches that the probes of SEQ ID NOs: 1-699,466 are derived from more than 24,000 full-length rat genes and EST clusters, and are chosen as predicted coding sequences from genomic BAC sequence entries (p.18 Ins.27-29).

The specification of the instant application asserts that claimed arrays can be used in the analysis of effects of a drug on gene expression (p.22), gene expression in response to selective environmental conditions (p.23 Ins.24-31), the study of genetic variation (p.24 Ins.25-29) and production of genetic maps and cross-species

comparison (p.25), characterize gene knockouts and identify new gene family members (p.26), and generate primers and ligands for specific genes (p.27).

The specification of the instant application provides no teaching as to what sort of genetic analysis would be required to draw any conclusion concerning any of the asserted uses of the claimed probe collections.

The asserted utilities of rat gene expression analysis are not considered specific or substantial because the disclosed uses of the nucleic acids of the array are not specific and are generally applicable to any nucleic acid. These non-specific uses are applicable to any nucleic acids and are not particular or specific to the nucleic acids and array being claimed. The array can be used to search for a utility, but significant unpredictable experimentation must be undertaken to establish an association between the probes and any particular phenotype such as drug effects or response to selective environmental conditions. Thus, there would be a burden on the artisan using the claimed product for the genetic analysis of rat to determine a specific and substantial utility for data generated by an analysis using the claimed invention. The asserted utilities, therefore, do not constitute a substantial utility for the claimed invention, since further experimentation would be required to establish a real world use for the claimed invention. Identifying and studying the properties of a compound itself or the mechanisms in which it is involved does not define a "real world" context or use. Neither the specification as filed nor any art of record discloses or suggests any property or activity for the nucleic acid such that another non-asserted utility would be well established for the claimed arrays.

Claims 1, 4-6, and 13-16 are also rejected under 35 U.S.C. 112, first paragraph.

Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1, 4-6, and 13-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is referred to the revised interim guidelines on written description published January 5, 2001 in the Federal Register, Volume 66, Number 5, page 1099-111 (also available at www.uspto.gov <<http://www.uspto.gov>>).

The claims are drawn to arrays of nucleic acid probes derived from rat genomic sequences. Claims 1 and 4-6 are drawn to arrays in which the probes comprise SEQ ID NOs: 1-699,466. Claims 13-16 are broadly drawn to arrays in which the probes are directed to at least 20,000 different rat transcripts.

When the claims are analyzed in light of the specification, the instant invention encompasses an enormous number of nucleic acid probes comprising a wide variety of

nucleic acid sequences. The claims are drawn to a plurality of nucleic acid probes that encompass an extremely large genus of full length genes, cDNAs, and variants (splice variants, polymorphisms and mutations including single and multiple nucleotide substitution, insertions, deletions, translocations and gene rearrangements). For claims 1 and 4-6, the claimed probes need only minimally comprise the recited 25 mers. Thus, while the disclosure teaches SEQ ID NO: 1-699,466, each disclosed SEQ ID NO is a unique fragments of the rat genome; and the claims encompass probes 'comprising' the disclosed SEQ ID NOs, which includes any nucleic acids containing any sequence additional to the disclosed SEQ ID NOs, such as, for example, full transcripts containing polymorphisms and mutations not taught by the instant specification. Claims 13-16 require no defining sequence information for the probes of the claimed array. Nucleic acids of such a large genus have not been taught by the specification. In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. The sequence listing of the instant application provides only SEQ ID NOs: 1-699,466. While the specification teaches that each of the disclosed sequences corresponds to and represents at least four additional nucleic acid sequences with one or more mismatches located anywhere in the disclosed sequences, the instant application does not provide any SEQ ID NOs other than SEQ ID NOs: 1-699,466.

Next, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (i.e. other than

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nucleotide sequence), specific features and functional attributes that would distinguish different members of the claimed genus. In the instant case, the specification does not provide any characteristics other than the nucleic acid sequences of SEQ ID NOs: 1-699,466.

Applicants' attention is directed to the decision in *In re Shokal*, 113 USPQ 283 (CCPA 1957) wherein is stated:

It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim. *In re Soll*, 25 C.C.P.A. (Patents) 1309, 97 F.2d 623, 38 USPQ 189; *In re Wahlfors* et al., 28 C.C.P.A. (Patents) 867, 117 F.2d 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of small genus such as the halogens, consisting of four species, a reduction to practice of three, or perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably larger number of reductions to practice would probably be necessary.

In the instant application, with the exception of an array comprising nucleic acid probes wherein each probe consists of one of SEQ ID NOs: 1-699,466, one of skill in the art cannot envision the detailed chemical structure of the encompassed polynucleotides, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required.

In conclusion, the limited information provided regarding SEQ ID NOs: 1-699,466 is not deemed sufficient to reasonably convey to one skilled in the art that Applicant is in possession of polynucleotide sequences besides those particularly disclosed in the specification at the time the application was filed.

Thus, having considered the breadth of the claims and the provisions of the specification, it is concluded that the specification does not provide adequate written

description for the claims.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1, 4, 13, and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Affymetrix Rat Genome U34 Set (Jan 2001).

Regarding claims 1 and 4, Affymetrix teaches a probe array (Rat Genome U34 Set, for example product number 900249) that is comprised of a plurality of probes interrogating greater than 24,000 mRNA transcripts and EST clusters from the UniGene database (p.2). Affymetrix further teaches that the array is in a GeneChip format, which is a solid support, relevant to claim 4.

The specification of the instant application teaches that the claimed SEQ ID NOs: 1-699,466 include more than 24,000 full-length rat genes and EST clusters from the UniGene database (p.18; p.32). Although the cited product reference does not specifically teach the sequences of SEQ ID NOs 1-699,466, this is considered an inherent property of the Rat Genome U34 Set. The MPEP in chapter 2100 states:

Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

In the examination of the instant application, based on the teachings of the instant specification, the PTO has basis for believing that the array Rat Genome U34 Set contains the sequences of SEQ ID NOS 1-699,466.

Regarding claims 13 and 15, the reference teaches that the probes interrogate greater than 24,000 mRNA transcripts, and that the array is in a GeneChip format, which is a solid support.

11. Claims 1; 4, 6, 13, 14, and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Gunther et al (1985).

Gunther et al teaches a Southern blot of rat genomic DNA on a nitrocellulose membrane.

Regarding claim 1, Gunther et al teaches a blot that contains genomic DNA isolated from rat liver (p.1258 – DNA preparation), digested with restriction enzymes, and transferred onto nitrocellulose (p.1258 – Restriction enzyme digestion, gel electrophoresis, blotting, and hybridization). The resulting membrane (Fig 2; Fig 3) thus contains a plurality of nucleic acid probes (the various restriction fragments) corresponding to the entire rat genome. Because of the comprehensive nature of the probes on the blot taught by Gunther et al (i.e. the blot is the entire rat genome), the plurality of probes on the southern blot inherently comprise each of the sequences listed in SEQ ID NO: 1-699,466, which are taught by the instant specification to be derived from rat genes.

Regarding claims 4 and 6, Gunther et al teaches a blot on nitrocellulose, which is a solid support. The reference further teaches that the genomic DNA from a rat is separated in a single lane of a gel and transferred to the nitrocellulose, thus the separated probes are on a single contiguous solid support (Fig 2; Fig 3).

Regarding claim 13 the Southern blot of Gunther et al (Fig 2; Fig 3) contains the entire rat genome, and probes for any and every transcript that results from the encoded genes. Thus the blot is an array of probes comprising probes to each of at least 20,000 different rat transcripts.

Regarding claims 14 and 16, Gunther teaches immobilized genomic DNA on a single piece of nitrocellulose, thus a single contiguous solid support. Additionally, nitrocellulose is a membrane.

12. Claims 13-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Brennan US Patent 5,474,796 (1995).

The rejected claims are broadly drawn to an array of probes comprising at least one probe to each of at least 20,000 different rat transcripts. Brennan teaches a microarray that contains 10-mer polynucleotides spotted at a discrete location such that the total array represents every possible permutation of 10-mer oligonucleotide (col. 9, Ins. 48-55).

Regarding claim 13, because of the comprehensive nature of the probe array taught by Brennan, such an array would inherently comprise nucleic acid probes to any possible rat transcript, including at least 20,000 different rat transcripts.

Regarding claims 14 and 15, Brennan teaches a hybridization array synthesized on a glass plate (Example 1, col.7), thus a single contiguous solid support that is a chip.

Regarding claim 16, Brennan also teaches the arrays on membranes (col.1 Ins.16-24).

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

14. Claims 5, 6, 14 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Affymetrix Rat Genome U34 Set (Jan 2001) in view of Fodor et al US Pat 6,309,822 (as cited in the IDS).

Affymetrix teaches a probe array (Rat Genome U34 Set, for example product number 900249) that is comprised of a plurality of probes interrogating greater than 24,000 mRNA transcripts and EST clusters from the UniGene database (p.2). Affymetrix further teaches that the array is in a GeneChip format, which is a solid support.

The specification of the instant application teaches that the claimed SEQ ID NOs: 1-699,466 include more than 24,000 full-length rat genes and EST clusters from the UniGene database (p.18; p.32). Although the cited product reference does not

specifically teach the sequences of SEQ ID NOS 1-699,466, this is considered an inherent property of the Rat Genome U34 Set. The MPEP in chapter 2100 states:

Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

In the examination of the instant application, based on the teachings of the instant specification, the PTO has basis for believing that the array Rat Genome U34 Set contains the sequences of SEQ ID NOS 1-699,466.

Affymetrix does not teach that the Rat Genome U34 Set comprise probes attached to a plurality of beads (claim 5), or that the array consists of a single contiguous solid support.

Fodor et al teaches nucleic acid probe arrays. The reference teaches that the oligonucleotides in an array can be provided attached to beads (col. 21), and teaches including individual probes attached to each bead (relevant to claim 4). Fodor teaches that there is a need to provide arrays of large numbers of oligonucleotide probes for gene expression analysis (col. 2), and further teaches that an array can comprise up to 1,000,000 different oligonucleotide probes (col. 15, lines 15-20) in less than 1 cm² (relevant to claim 6).

Regarding claims 14, Fodor et al teaches that probe density of an array can comprise up to 1,000,000 different oligonucleotide probes (col. 15, lines 15-20) in less than 1 cm².

Regarding claim 16, Fodor et al teaches membranes as solid supports for probe arrays (col. 95).

It would have been prima facie obvious to one of skill in the art to have modified the Rat Genome U34 Set array of Affymetrix so as to have incorporated the teachings of Fodor et al. Such modifications would have included providing the probes of the array on a plurality of beads and membranes, as well as providing the probes on a single contiguous solid support. One would have been motivated to create such arrays because Fodor et al teaches such products for the analysis of gene expression.

15. Claims 1, 4-6, 13-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rat UniGene Build 34 (1998) in view of Fodor et al US Pat 6,309,822 (as cited in the IDS).

The claims are drawn to arrays of nucleic acid probes. Claims 1 and 4-6 are drawn to arrays of probes wherein the probes comprise SEQ ID NO: 1-699,466. Claim 4 requires that the probes are attached to a solid support, claim 5 requires that the probes are attached to beads, and claim 6 requires that the array consist of a single contiguous solid support. Claims 13-16 require no defining sequence information for the probes of the claimed arrays. Claim 13 is drawn to an array of probes to at least 20,000 different rat transcripts. Claim 14 requires that the probes are attached to a single contiguous solid support, claim 15 requires that the support is a chip, and claim 16 requires that the support is a membrane.

Rat UniGene Build 34 teaches the sequences of genes and ESTs from rat (Affymetrix 2001 catalog, and Email from NCBI). Build 34 teaches sequences information regarding greater than 24,000 mRNA transcripts and EST clusters (relevant to claims 13-16). Absent evidence to the contrary, the Build 34, is taken to provide the sequence information of SEQ ID NOS 1-699,466 (relevant to claims 1, and 4-6). The UniGene database does not teach probes comprising each of SEQ ID NOs 1-699,466.

Fodor teaches arrays of oligonucleotide probes for gene expression analysis (col 2).

Regarding claim 1, Fodor teaches that the array can comprise up to 1,000,000 different oligonucleotide probes (col. 15, lines 15-20) in less than 1 cm², wherein sets of probes are chosen to be complementary over a gene sequence (col. 14). The reference teaches that particularly preferred probes have lengths from about 20 to about 25 nucleotides in length, and has multiple oligonucleotide probes complementary to each gene (col. 3)

Regarding claims 4 and 5, Fodor teaches that the oligonucleotides in the array can be provided attached to beads (col. 21), including individual probes attached to each bead.

Regarding claim 6, Fodor et al teaches that probe density of an array can comprise up to 1,000,000 different oligonucleotide probes (col. 15, lines 15-20) in less than 1 cm².

Regarding claim 13, Fodor teaches that sets of probes are chosen to be complementary over a gene sequence (col. 14).

Regarding claims 14, Fodor et al teaches that probe density of an array can comprise up to 1,000,000 different oligonucleotide probes (col. 15, lines 15-20) in less than 1 cm².

Regarding claim 15, Fodor et al teaches microfabricated arrays of large numbers of different oligonucleotide probes, which are DNA chips (col.2)

Regarding claim 16, Fodor et al teaches membranes as solid supports for probe arrays (col. 95).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have used the gene and EST sequence information of Rat UniGene Build 34 to have constructed nucleotide probe arrays as taught by Fodor et al. Such an array would have included probe sets for genes and ESTs in the UniGene database for the purpose of providing an array of probes for gene expression analysis as taught by Fodor. The ordinary artisan would have been motivated to provide an array of probe sets for rat sequences because Fodor teaches arrays for gene expression monitoring.

16. Claims 1, 4-6, 13-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rat UniGene Build 99 (June 2002) in view of Fodor et al US Pat 6,309,822 (as cited in the IDS).

The claims are drawn to arrays of nucleic acid probes. Claims 1 and 4-6 are drawn to arrays of probes wherein the probes comprise SEQ ID NO: 1-699,466. Claim 4 requires that the probes are attached to a solid support, claim 5 requires that the

probes are attached to beads, and claim 6 requires that the array consist of a single contiguous solid support. Claims 13-16 require no defining sequence information for the probes of the claimed arrays. Claim 13 is drawn to an array of probes to at least 20,000 different rat transcripts. Claim 14 requires that the probes are attached to a single contiguous solid support, claim 15 requires that the support is a chip, and claim 16 requires that the support is a membrane.

Rat UniGene Build 99 (as disclosed in the Data Sheet for Affymetrix Rat Genome 230 Arrays, page 2) teaches the sequences of genes and ESTs from rat. Build 99 teaches sequences information regarding greater than 24,000 mRNA transcripts and EST clusters (relevant to claims 13-16). Absent evidence to the contrary, the Build 99, is taken to provide the sequence information of SEQ ID NOS 1-699,466 (relevant to claims 1, and 4-6). The UniGene database does not teach probes comprising each of SEQ ID NOs 1-699,466.

Fodor teaches arrays of oligonucleotide probes for gene expression analysis (col 2).

Regarding claim 1, Fodor teaches that the array can comprise up to 1,000,000 different oligonucleotide probes (col. 15, lines 15-20) in less than 1 cm², wherein sets of probes are chosen to be complementary over a gene sequence (col. 14). The reference teaches that particularly preferred probes have lengths from about 20 to about 25 nucleotides in length, and has multiple oligonucleotide probes complementary to each gene (col. 3)

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Regarding claims 4 and 5, Fodor teaches that the oligonucleotides in the array can be provided attached to beads (col. 21), including individual probes attached to each bead.

Regarding claim 6, Fodor et al teaches that probe density of an array can comprise up to 1,000,000 different oligonucleotide probes (col. 15, lines 15-20) in less than 1 cm².

Regarding claim 13, Fodor teaches that sets of probes are chosen to be complementary over a gene sequence (col. 14).

Regarding claims 14, Fodor et al teaches that probe density of an array can comprise up to 1,000,000 different oligonucleotide probes (col. 15, lines 15-20) in less than 1 cm².

Regarding claim 15, Fodor et al teaches microfabricated arrays of large numbers of different oligonucleotide probes, which are DNA chips (col. 2)

Regarding claim 16, Fodor et al teaches membranes as solid supports for probe arrays (col. 95).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have used the gene and EST sequence information of Rat UniGene Build 99 to have constructed nucleotide probe arrays as taught by Fodor et al. Such an array would have included probe sets for genes and ESTs in the UniGene database for the purpose of providing an array of probes for gene expression analysis as taught by Fodor. The ordinary artisan would have been motivated to

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provide an array of probe sets for rat sequences because Fodor teaches arrays for gene expression monitoring.

It is noted that the specification of the instant application indicates that the probes of the instant invention are derived from the Rat UniGene database (build 99) (page 32).

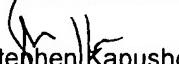
Conclusion

17. No claim is allowable. No claim is free of the prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Kapushoc whose telephone number is 571-272-3312. The examiner can normally be reached on Monday through Friday, from 8am until 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


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